AR201-13403A

(19-December-2001)

RECEIVED
OPPT NCIC
2001 DEC 27 AM 9:49

ROBUST SUMMARY FOR HCFC-123

Summary

HCFC-123 is soluble in water (1488 mg/L at 25°C), has a melting point of -107°C, and boils at 27.8°C. HCFC-123 is a clear, colorless liquid with a slight ether odor, and has a vapor pressure of 13.24 psia at 25°C. The estimated log octanol-water partition coefficient of HCFC-123 is 2.307.

HCFC-123 is used as a refrigerant and as an intermediate in the production of trifluoroacetylchloride, various agricultural chemicals, HCFC-124, and HFC-125. It may be released to the environment as a fugitive emission during its production or use. If released to water, HCFC-123 will rapidly volatilize to the atmosphere. The estimated half-life for volatilization from a model river is 3.6 hours. HCFC-123 is not expected to bioconcentrate in fish and aquatic organisms or adsorb to sediment or suspended organic matter. If released to the atmosphere, HCFC-123 will undergo a slow gas-phase reaction with photochemically produced hydroxyl radicals. The atmospheric lifetime of HCFC-123 has been estimated to range from 1.2 to 2.4 years. HCFC-123 may undergo atmospheric removal by wet deposition processes; however, any compound removed by this process is expected to rapidly re-volatilize to the atmosphere (SRC, n.d.). Closed bottle studies with activated sludge indicate this compound is not readily biodegradable.

HCFC-123 exhibits slight to moderate toxicity to fish, invertebrates, and algae. HCFC-123 exhibited a 96-hour LC_{50} of 55.5 mg/L in rainbow trout, a 48-hour EC_{50} of 17.3 mg/L in *Daphnia*, and a 96-hour EC_{50} of 67.8 and 96.6 mg/L for biomass and average specific growth, respectively, in algae.

HCFC-123 exhibits very low toxicity in acute tests with an oral ALD in rats of 9000 mg/kg and a 4-hour inhalation LC_{50} of 32,000 ppm in rats. The dermal LD_{50} in rats and rabbits was >2000 mg/kg. HCFC-123 was not irritating to rabbit skin, produced mild to severe eye irritation in rabbits, and was not a sensitizer to guinea pig skin. In a cardiac sensitization study in dogs, an EC_{50} value of 19,500 ppm was determined.

In a 2-year inhalation study in rats, a no-observable-effect level was not achieved (rats received 0, 300, 1000, or 5000 ppm) based on effects in clinical chemistry parameters at 300, 1000, and 5000 ppm, lower body weight and body weight gain at 300, 1000, and 5000 ppm, higher liver weights at 5000 ppm, increased incidence of neoplastic and non-neoplastic morphological changes, and higher hepatic peroxisomal β-oxidation activity at all concentrations. The peroxisome proliferation, beta-oxidation related effects on clinical chemistry, liver hypertrophy, and tumors were considered to be rodent specific and of low-to-no risk to humans. No developmental toxicity was observed in rabbits (administered up to 5000 ppm) or rats (administered up to 10,000 ppm). In a 2-generation reproduction study in rats, exposure to HCFC-123 was principally associated with peroxisome proliferation related effects on growth and on the liver. It was not possible to identify a no-effect level as effects were seen in some

parameters at the lowest exposure level (30 ppm). In terms of reproductive performance, the only adverse finding was decreased implantation counts among F_1 females at 1000 ppm. In terms of development, all exposure levels (30, 100, 300, and 1000 ppm) were associated with impaired pup growth in the offspring of the F_1 generation. Since HCFC-123 and/or its metabolite trifluoroacetic acid are present in milk consumed by nursing pups, the decrease in pup weights was secondary to hepatic peroxisome proliferation.

HCFC-123 was non-mutagenic when tested in the *in vitro* bacterial reverse mutation test. However, HCFC-123 was positive for clastogenicity in three independently conducted *in vitro* chromosome aberration tests. All three tests were positive for the induction of structural chromosome aberrations in the 24-hour exposure without S-9 metabolic activation. One test was also positive in the 3-hour exposure with S-9 metabolic activation. A dose-related increase in the amount of numerical aberrations (polyploidy) was also cautiously noted in this study in the 3-hour exposure without S-9 metabolic activation.

When tested *in vivo*, HCFC-123 was negative in the mouse micronucleus test, negative in the unscheduled DNA synthesis assay, and negative in the *in vivo* chromosome aberration assay.

There is a significant database on the human exposure to varying concentrations of HCFC-123. In HCFC-123 production workers, exposures are consistently below 1-2 ppm HCFC-123 for an 8-hour time-weighted average (TWA) concentration. In an industrial hygiene monitoring campaign in 2000 at an HCFC-123 manufacturing facility, the maximum TWA concentrations were 1.49 ppm for an area monitor near a drum filling operation and 3.09 ppm for a person working in the facility. DuPont has no data on exposure to HCFC-123 during its use as a chemical intermediate. However, each of the processes where HCFC-123 is used as an intermediate is a closed system, and exposure should be much less than established exposure limits.

Extensive data exist for refrigerant system operation and maintenance. Emissions monitoring during the past six years has shown that properly maintained and operated HCFC-123 chillers have refrigerant emissions levels of 0 to 1 ppm in air. Recognizing that HCFC-123 can induce liver toxicity if one is over-exposed, the American Society of Heating, Refrigerating, and Air Conditioning Engineers (ASHRE) has established in Standard 15 that area monitors in refrigeration machinery rooms are required for systems containing HCFC-123. DuPont also recommends that HCFC-123 specific air monitor be installed and maintained in all indoor applications to ensure that there is sufficient warning in the event of a refrigerant leak. NICNAS (NICNAS, 1996) states “Chiller workers, although potentially exposed on a routine basis, are unlikely to be exposed to levels (airborne) in excess of 5 ppm (TWA) and hence the risk of chronic health effects is considered low.”

In addition to the uses previously listed, HCFC-123 had been used as a specialty cleaning agent as an alternative to CFC-113. However, environmental monitoring in typical cleaning operations has shown that exposure to workers is very difficult to control to levels below the established exposure limit of 50 ppm (8-hour TWA) set by the American Industrial Hygiene Association (AIHA) Workplace Environmental Exposure Limit (WEEL) Committee. Concentrations in

vapor degreasing operations have shown 4-10 ppm background levels when the operation is not taking place to as high as 810 ppm in an application where the condensing unit was undersized. As a result, HCFC-123 ceased to be sold into cleaning agent applications and other applications where it was handled in open systems.

There have been several cases where liver toxicity has been reported upon exposure to HCFC-123 in the workplace. As noted in the WEEL Guide (AIHA, 2001), "A common theme for all of the documented human liver disease cases associated with HCFC-123 is the lack of concurrent exposure measurement with adverse health effects and poor industrial hygiene practices. In all of the cases cited, it is probably that exposures were very high for undetermined periods of time." In cases where the exposure scenario was modeled or recreated (Omae et al., 2000), levels that caused liver effects were much higher than established exposure limits when calculated or measured.

Liver toxicity has not been reported in workers where appropriate industrial hygiene measures and/or personal protective equipment has been used to ensure compliance with the 50 ppm 8-hr TWA exposure limit set by the AIHA WEEL Committee (DuPont, 1998a; 1998b; 1999).

References for the Summary:

AIHA (2001). Workplace Environmental Exposure Level (WEEL) Guide, American Industrial Hygiene Association, Fairfax, VA.

DuPont Co. (1998a). "Personal Communication from G. Malinverno to W. Brock," August, 1998 [Private Conversation], E. I. du Pont de Nemours & Co., Haskell Laboratory, 1090 Elkton Road, Newark, DE 19714 (cited in AIHA (2001). Workplace Environmental Exposure Level (WEEL) Guide, American Industrial Hygiene Association, Fairfax, VA).

DuPont Co. (1998b). "Personal Communication from P. Hoy to W. Brock," August 6, 1998 [Private Conversation], E. I. du Pont de Nemours & Co., Haskell Laboratory, 1090 Elkton Road, Newark, DE 19714 (cited in AIHA (2001). Workplace Environmental Exposure Level (WEEL) Guide, American Industrial Hygiene Association, Fairfax, VA).

DuPont Co. (1999). "Personal Communication from T. McCain to H. J. Trochimowicz," September 21, 1990 [Private Conversation], E. I. du Pont de Nemours & Co., Haskell Laboratory, 1090 Elkton Road, Newark, DE 19714 (cited in AIHA (2001). Workplace Environmental Exposure Level (WEEL) Guide, American Industrial Hygiene Association, Fairfax, VA).

NICNAS (1996). Priority Existing Chemical, Vol. 4, 119 p.

Omae, K. et al. (2000). J. Occup. Health, 42(5):235-238 (BIOSIS/2001/42205).

SRC (n.d.). Syracuse Research Corporation (HSDB/6752).

(19-December-2001)

TEST PLAN FOR HCFC-123

HCFC-123 **CAS No. 306-83-2**	**Data Available**	**Data Acceptable**	**Testing Required**
	Y/N	**Y/N**	**Y/N**
PHYSICAL/CHEMICAL CHARACTERISTICS			
Melting Point	Y	Y	N
Boiling Point	Y	Y	N
Vapor Pressure	Y	Y	N
Partition Coefficient	Y	Y	N
Water Solubility	Y	Y	N
ENVIRONMENTAL FATE			
Photodegradation	Y	Y	N
Stability in Water	Y	Y	N
Transport (Fugacity)	Y	Y	N
Biodegradation	Y	Y	N
ECOTOXICITY			
Acute Toxicity to Fish	Y	Y	N
Acute Toxicity to Invertebrates	Y	Y	N
Acute Toxicity to Aquatic Plants	Y	Y	N
MAMMALIAN TOXICITY			
Acute Toxicity	Y	Y	N
Repeated Dose Toxicity	Y	Y	N
Developmental Toxicity	Y	Y	N
Reproductive Toxicity	Y	Y	N
Genetic Toxicity Gene Mutations	Y	Y	N
Genetic Toxicity Chromosomal Aberrations	Y	Y	N